UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ARTHUR A. GERTZMAN and MOON HAE SUNWOO

Appeal 2007-0532
Application 10/828,316
Technology Center 1600

Decided: March 27, 2007

Before TONI R. SCHEINER, ERIC GRIMES, and NANCY J. LINCK, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a bone repair composition. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

BACKGROUND

The specification discloses "a composition for filling bone defects using demineralized allograft bone particles . . . mixed in a fluid carrier having an isotonic phosphate buffer and a high molecular weight viscous

excipient derived from the class of biomaterials known as hydrogels which contains cell material and/or growth factors" (Specification 1).

DISCUSSION

1. CLAIMS

Claims 2, 7, 8, and 21-28 are pending and on appeal. The claims have been argued in three groups; the claims within these groups will stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claims 21, 23, and 26 are representative and read as follows:

21. A sterile formable bone composition for application to a bone defect site to promote new bone growth at the site comprising a demineralized osteoinductive and osteoconductive bone particles in an aqueous carrier solution, the bone particles being added to a viscous carrier at a concentration ranging from 5-50%(w/w), the carrier comprising a hydrogel taken from a group consisting of chitosan and sodium alginate in a phosphate buffered aqueous solution, said hydrogel ranging from about 5.0% to about 20.0% by weight of the aqueous carrier solution and said hydrogel component having a molecular weight ranging from ten thousand to three hundred thousand Daltons with a stable viscosity at a temperature ranging from about 22° C to about 37° C and said composition having a pH ranging from about 6.8 to about 7.4 and a growth factor additive added to said composition, said growth factor comprising one or more of a group consisting of transforming growth factor (TGF-beta), insulin growth factor (IGF-1)); plat[e]let derived growth factor (PDGF), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF)(numbers 1-23), osteopontin, growth hormones such as somatotropin cellular attractants and attachment agents.

23. A sterile formable bone composition for application to a bone defect site to promote new bone growth at the site comprising demineralized osteoinductive and osteoconductive allograft bone particles in an aqueous carrier solution, the bone particles being added to a viscous carrier at a concentration ranging from 5-50%(w/w), the carrier comprising a chitosan in a phosphate buffered aqueous solution, said hydrogel chitosan ranging from about 5.0% to about 20.0% by weight of the aqueous carrier solution

and cellular material taken from a group consisting of living cells, cell elements such as red blood cells, white blood cells, platelets, blood plasma, pluripotential cells, osteoblasts, osteoclasts, and fibroblasts, epithelial cells, and endothelial cells present at a concentration of 10^5 to 10^8 per cc of the carrier, said hydrogel component having a molecular weight ranging from ten thousand to three hundred thousand Daltons with a stable viscosity and said composition having a pH ranging from about 6.8 to about 7.4[.]

26. A sterile formable bone composition as claimed in claim 23 wherein said bone particles are allograft cortical bone ranging from 100 microns to 850 microns in size at a concentration ranging from 20% to 35% by weight of the composition.

Claim 21 is directed to a formable composition comprising demineralized bone particles (5-50% w/w) in a viscous, phosphate buffered aqueous carrier. The carrier contains either chitosan or sodium alginate (5-20% by weight of the carrier) with a molecular weight of 10,000 to 300,000 Daltons and provides a stable viscosity at 22° C to 37° C. The composition also has a pH in the range of 6.8 to 7.4 and comprises at least one of "transforming growth factor (TGF-beta), insulin growth factor (IGF-1), plat[e]let derived growth factor (PDGF), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) (numbers 1-23), osteopontin, growth hormones such as somatotropin cellular attractants and attachment agents."

Claim 23 is directed to a similar composition but requires chitosan as the hydrogel, does not require a growth factor, and requires a "cellular material taken from a group consisting of living cells, cell elements such as red blood cells, white blood cells, platelets, blood plasma, pluripotential cells, osteoblasts, osteoclasts, and fibroblasts, epithelial cells, and

endothelial cells present at a concentration of 10^5 to 10^8 per cc of the carrier."

Claim 26 depends on claim 23 and limits the bone particles to allograft cortical bone in the size range of 100-850 microns and in a concentration of 20-35% by weight.

Claims 21 and 23 both state, in the preamble, that the composition is "for application to a bone defect site to promote new bone growth at the site." This preamble language merely recites the intended use of the composition; it does not add any limitations to those recited in the body of the claim. Therefore, we give it no weight in interpreting the claim. *See, e.g., IMS Technology, Inc. v. Haas Automation, Inc.*, 206 F.3d 1422, 1434, 54 USPQ2d 1129, 1137 (Fed. Cir. 2000) ("If the preamble adds no limitations to those in the body of the claim, the preamble is not itself a claim limitation and is irrelevant to proper construction of the claim.").

Both claims 21 and 23 also state that the demineralized bone particles are "osteoinductive and osteoconductive."[1] This language, as well, does not further limit the claims because it merely recites inherent properties of demineralized bone particles. The instant specification itself states that the "demineralized form of allograft bone is naturally both osteoinductive and osteoconductive." Therefore, all demineralized bone particles are "demineralized osteoinductive and osteoconductive bone particles."

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[1] "Osteoinduction and osteoconduction are two mechanisms by which a graft may stimulate the growth of new bone. In the former case, inductive signals of a little-understood nature lead to the phenotypic conversion of connective tissue cells to bone cells. In the latter, the implant provides a scaffold for bony ingrowth." Breitbart, US 5,700,289, col. 1, ll. 36-42 (of record).

2. OBVIOUSNESS

Claims 2, 7, 8, and 21-28 stand rejected under 35 U.S.C. § 103 as obvious in view of Boyce,[2] Breitbart,[3] and Sander.[4] The Examiner relies on Boyce for its disclosure of an "osteoimplant composition comprising bone particles in physiological saline" (Answer 4). The Examiner also notes that Boyce teaches that the composition can contain "chitosan and hydrogels" as well as "bioactive substances" (*id.*).

The Examiner relies on Breitbart for teaching a "bone repair composition comprising cells such as stem cells, chondrocytes and mesenchyma cells," and relies on Sander for "disclosing a composition suitable for bone repair comprising biocompatible particles dispersed in a matrix" (*id.* at 5). The Examiner concludes that "[o]ne of ordinary skill in the art would be motivated to prepare a composition comprising bone particles and bioactive agents having osteoinductive properties such as growth factors to form a bone cement composition as disclosed in the prior art cited" (*id.*).

We agree with the Examiner that the compositions of claims 21, 23, and 26 would have been obvious to a person of ordinary skill in the art based on the cited references. Boyce discloses a composition for making osteoimplants (col. 4, ll. 26-32). The composition contains bone particles that can be demineralized (col. 5, ll. 37-39) in an amount of "about 5 to about 100 weight percent" (col. 7, ll. 48-50).

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[2] Boyce, US 6,294,187 B1, Sep. 25, 2001.
[3] Breitbart, US 5,700,289, Dec. 23, 1997.
[4] Sander, US 5,356,629, Oct. 18, 1994.

Boyce states that the "bone particles can be combined with one or more biocompatible components such as *wetting agents*, *biocompatible binders*, *fillers*, fibers, plasticizers, biostatic/biocidal agents, surface active agents, *bioactive agents*, and the like, prior to, during, or after compressing the bone particle-containing composition" (col. 7, ll. 55-60) (emphasis added).

Boyce discloses that suitable wetting agents include physiological saline (col. 7, l. 66 to col. 8, l. 1). Boyce does not expressly state that the physiological saline is phosphate buffered, but Appellants do not argue that there is a patentable distinction between Boyce's "physiological saline" and the "phosphate-buffered aqueous solution" recited in the claims.

Boyce states that suitable bioactive binders include chitosan (col. 8, ll. 13-16). "When employed, binders will typically represent from about 5 to about 70 weight percent of the bone particle-containing composition, calculated prior to compression of the composition" (Boyce, col. 8, ll. 37-40). Boyce also states that chitosan can be added as a thickener when bone particles show a tendency to settle out of a particular slurry or paste composition (col. 10, l. 58 to col. 11, l. 9).

Boyce discloses that preferred fillers include demineralized bone powder and that, "[w]hen employed, filler will typically represent from about 5 to about 80 weight percent of the bone particle-containing composition, calculated prior to compression of the composition" (col. 8, ll. 55-58).

Boyce also discloses that

> [b]ioactive substances which can be readily combined with the bone particles include . . . living cells such as chondrocytes,

> bone marrow cells, mesenchymal stem cells, . . . autogenous tissues such as blood, serum, . . . human growth hormone (HGH); . . . transforming growth factor (TGF-beta); insulin-like growth factor (IGF-1); platelet derived growth factors (PDGF); fibroblast growth factors (FGF, bFGF, etc.), . . . [and] somatotropin."

(Col. 9, ll. 31-62).

Finally, Boyce discloses that the bone particle-containing composition can be fabricated by wetting a quantity of bone particles with a wetting agent "to form a composition having the consistency of a slurry or paste. Optionally, the wetting agent can comprise dissolved or admixed therein one or more biocompatible substances such as biocompatible binders, fillers, plasticizers, biostatic/biocidal agents, surface active agents, bioactive substances, etc., as previously described" (col. 10, ll. 20-30).

Breitbart discloses a method of obtaining cells from periosteum (the covering around the surface of the bone) and seeding them onto a matrix for repair of a bone defect (col. 3, ll. 24-26). Breitbart discloses that hydrogel matrices can be used (col. 3, ll. 34-35) and that the matrix can be formed from alginate (col. 6, ll. 19-38), optionally stabilized with a polycation such as chitosan (col. 11, ll. 27-37).

Sander discloses a bone repair composition comprising a matrix having biocompatible particles dispersed in it (col. 2, ll. 1-4). The biocompatible particles can be bone particles (col. 4, ll. 12-15), preferably with an average size of 0.1 to 3 mm (i.e., 100 to 3000 microns) but "even as small as about 100 to 700 microns" (col. 4, ll. 33-38). Sander also teaches incorporating growth promoting factors such as FGF or PDGF into the bone repair composition (col. 4, l. 51 to col. 5, l. 5).

We agree with the Examiner that the cited references would have made obvious the compositions of claims 21, 23, and 26 to a person of ordinary skill in the art. Specifically, Boyce discloses a composition comprising bone particles in a carrier, at a concentration of at least 5%, and suggests using demineralized bone particles (col. 5, ll. 37-39; col. 7, ll. 48-50). Boyce also suggests adding chitosan to the composition as a binder or thickener in an amount of 5-80% (col. 8, ll. 13-16 and ll. 37-40; col. 10, l. 58 to col. 11, l. 9).

Boyce also suggests adding bioactive substances to the composition, including various cells, blood, and growth factors such as TGF-beta (col. 9, ll. 31-62). Similarly, Sander suggests adding growth factors such as fibroblast growth factor (FGF) to a bone repair composition (col. 4, l. 51 to col. 5, l. 5).

Boyce suggests mixing the bone particles with a wetting agent and additives to form a "composition having the consistency of a slurry or paste" (col. 10, ll. 20-30); i.e., a formable composition. Boyce teaches that suitable wetting agents include physiological saline (col. 8, l. 1), which would have suggested phosphate-buffered saline (PBS) to those of skill in the art.

We agree with the Examiner that, based on these disclosures, a person of ordinary skill in the art would have found it obvious to make a composition comprising 5-50% demineralized bone particles in phosphate buffered saline combined with chitosan (5-20% by weight) and a growth factor such as TGF-beta or a cellular material such as blood serum (plasma).

The references do not expressly disclose the molecular weight range recited in the claims. Appellants, however, did not challenge the Examiner's

position that "the molecular weight of the instant application is within the matrix molecular weight used by [Sander] and Boyce" (Answer 12).

The references also do not expressly disclose the pH range recited in the claims, nor does Boyce characterize the viscosity of the slurry or paste composition at 22° C and 37° C. Again, however, Appellants do not argue that either of these limitations distinguishes the claimed composition from the one suggested by the cited references.

We also agree that the cited references would have suggested the composition of claim 26, which adds to claim 23 the limitation that the bone particles have a size range of 100 to 850 microns (i.e., 0.1 to 0.85 mm) and a concentration of 20-35% of the composition. Boyce teaches a composition having 5-100% bone particles and therefore teaches a concentration range that overlaps the one recited in claim 26. With respect to the particle size range, Boyce teaches that the "powdered bone particles can range in average particle size from about 0.05 to about 1.2 cm" (col. 4, ll. 56-58), i.e., 0.5 to 12 mm. Thus, the range of particle sizes taught by Boyce also overlaps the size range recited in claim 26. "[W]here there is a range disclosed in the prior art, and the claimed invention falls within that range, there is a presumption of obviousness." *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322, 73 USPQ2d 1225, 1228 (Fed. Cir. 2004).

Appellants argue that Boyce teaches a "*shaped hardened load bearing osteoimplant bone structure formed of compressed bone particles* and not a . . . formable putty composition" (Br. 5, 14).

This argument is not persuasive. Boyce teaches that a composition having the consistency of a slurry or putty is formed, comprising all of the

elements recited in the instant claims, and that the formable composition is then further treated to make a load-bearing implant. The fact that Boyce subjects the disclosed formable composition to further treatment, however, does not prevent the disclosure of that composition from making the instant claims unpatentable under 35 U.S.C. § 103.

Appellants also argue that Boyce's working examples do not teach many of the limitations of the instant claims (Br. 7, 16) but that is irrelevant to an inquiry into obviousness. "[I]n a section 103 inquiry, 'the fact that a specific [embodiment] is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be considered.'" *Merck & Co. v. Biocraft Labs. Inc.*, 874 F.2d 804, 807, 10 USPQ2d 1843, 1846 (Fed. Cir. 1989).

Appellants argue that neither Sander nor Breitbart disclose all of the limitations of the instant claims (Br. 8-12, 17-21) but the rejection is based on the teachings of the combined references. "Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references." *In re Merck & Co.*, 800 F.2d 1091, 1097, 231 USPQ 375, 380 (Fed. Cir. 1986).

Appellants also argue that "none of the cited references disclose the additives of cells at a concentration of $10^5 - 10^8$ per cc of carrier or a specific amount of growth factor added to 10cc of carrier" (Br. 12, 21).

This argument is irrelevant to claim 21, which requires no particular concentration of growth factor, and it is unclear to what extent it has application to claim 23. Claim 23 requires a "cellular material taken from a group consisting of living cells, cell elements *such as* red blood cells, white

blood cells, platelets, blood plasma, pluripotential cells, osteoblasts, osteoclasts, *and* fibroblasts, epithelial cells, and endothelial cells present at a concentration of $10^5 - 10^8$ per cc of the carrier" (emphasis added). The emphasized elements of the claim make it unclear what part(s) of the list the "$10^5 - 10^8$ per cc" limitation applies to.

We need not labor over the question, however. The "cell elements" recited in claim 23 include "blood plasma" and Boyce suggests including "blood" in its composition. Since blood plasma does not have a concentration measured in units/cc, it is apparent that the "$10^5 - 10^8$ per cc" limitation does not apply to that element of claim 23. Boyce's "blood" includes "blood plasma" as one of its constituents, and Boyce therefore suggests a composition meeting the limitations of claim 23.

With respect to claim 26, Appellants argue that "the characterization of the Examiner that the sizes of the bone particles used in Boyce . . . correspond to that of the present invention is not correct," and none of the cited references teach the particle size range recited in the claim (Br. 23-24).

This argument is also unpersuasive. As discussed above, Boyce teaches particles that can be "relatively fine powders," ranging in size from 0.5 to 12 mm and having a length-to-thickness ratio of, e.g., 1:1 (col. 4, ll. 55-60). Claim 26 recites a size range of 100 to 850 microns, or 0.1 to 0.85 mm. The claimed size range therefore overlaps the size range disclosed by Boyce. "[W]here there is a range disclosed in the prior art, and the claimed invention falls within that range, there is a presumption of obviousness. But the presumption will be rebutted if it can be shown: (1) That the prior art taught away from the claimed invention; or (2) that there

are new and unexpected results relative to the prior art." *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1322, 73 USPQ2d 1225, 1228 (Fed. Cir. 2004) (citations omitted). Appellants have not rebutted the presumption of obviousness arising from the overlapping ranges.

SUMMARY

We affirm the rejection under 35 U.S.C. § 103 of claims 21, 23, and 26. Claims 2, 7, 8, 22, 24, 25, 27, and 28 fall with the representative claims.

AFFIRMED

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JOHN S. HALE
GIPPLE & HALE
6665-A OLD DOMINION DRIVE
MCLEAN VA 22101